REMARKS/ARGUMENT

Claims 7-12 have been amended to overcome the Examiner's objection to these claims and claims 15 et seq. have been revised to indicate that the combination is a pharmaceutical dosage unit. The two compositions exert the desired effect when used in combination, i.e., when administered simultaneously or in close temporal relationship but for stability reasons, they cannot be merged into a single physical entity. The rejection of claims 15-19 under 35 U.S.C. § 101 has therefore been rendered moot. The carrier referred to in claim 16 and 17 refer to both carriers and this has been made clear. None of these changes has diminished the scope of the claims in any way.

Two claims corresponding to claims 1-3 but specifying the ammonium as ammonium chloride (see claim 19) have been presented for consideration by the Examiner.

The rejection of claims 15-19 under 35 U.S.C. § 112, second paragraph, as being indefinite in not reciting the amount effective is respectfully traversed. There is nothing wrong with expressing an amount in functional terms and there is more than sufficient disclosure in the application to guide those skilled in the art to determine, without undue experimentation, what amount is sufficient to preserve skeletal muscle. See, e.g., In re Halleck, 164 U.S.P.Q. 647 (C.C.P.A. 1970) ("an effective amount" is not objectionable where artisan can determine from written disclosure and examples what an effective amount constitutes).

The rejection of claims 1-6 and 15-17 under 35 U.S.C. § 102 over Veech and the rejection of the remaining original claims under 35 U.S.C. § 103 over the same reference is respectfully traversed. The claimed invention is neither taught nor suggested by this reference.

The Veech patent relates to parenteral nutritional compositions "which contain the major plasma amino acids". The formulation thus contains at least one metabolizable nitrogen compound set forth in Table 5 of the reference, at least one carboxylic metabolite anion which can be α-ketoglutarate and at least one cation which can be ammonium. These formulations are said to achieve normalized redox balance within the organs of animals to which they are administered, thereby controlling or normalizing the cellular phosphorization state. The formulation may additionally contain optional ingredients including, for example, glutamine. Nevertheless, it is clear from the disclosure of Veech that the metabolizable nitrogen-containing

compounds appearing in Table 5 and designated as component (A) -- see column 5 -- are essential to these formulations and effects the basic properties of the formulations. The scope of claim 1 as amended herein excludes the Table 5 metabolizable nitrogen-containing compounds. Accordingly, claim 1 and the claims dependent on it are not anticipated by Veech. There is nothing in the reference that teaches or suggests that the Table 5 compounds can be replaced and indeed to do so would destroy the Veech formulations. Clearly, therefore, there is no suggestion of the claim 1 compositions in the reference.

It will also be appreciated that in contrast to Veech, the present invention points to the fact that the direct administration of a material such as glutamine to a patient in a state of glutamine depletion is not an optimal way of coping with such deficiency. Glutamine is not soluble in water and cannot be sterilized by autoclavation (page 2, last paragraph). The present invention provides an improved method of preserving bodily protein stores, that is, to prevent skeletal muscle from being used as a source of free glutamine in a condition of glutamine deficiency such as in a catabolic patient.

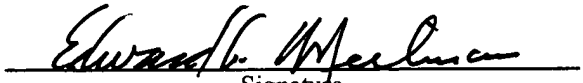
With regard to new claims 20 and 21, it is respectfully pointed out that Veech emphasizes that is compositions are non-hypochloremic (column 5, line 40). That is, they do not supply chloride ion to the body. This problem is discussed in more detail in the paragraph spanning columns 14 and 15 of the reference. To present a composition containing chloride ion is, therefore, directly contrary to the reference. Claims 20 and 22 do present a composition containing chloride ion. Accordingly, Veech cannot provide a basis for questioning the patentability of these additional claims.

In light of all of the foregoing considerations, it is respectfully submitted that this application is now in condition to be allowed and the early issuance of a notice of allowance is respectfully solicited.

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to: Asst. Commissioner for Patents, Washington, D.C. 20231, on July 10, 2001:

Edward A. Meilman

Name of applicant, assignee or Registered Representative



Signature

July 10, 2001

Date of Signature

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Respectfully submitted,

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APPENDIX A

"CLEAN" VERSION OF EACH PARAGRAPH/SECTION/CLAIM
37 C.F.R. § 1.121(b)(ii) AND (c)(i)

SPECIFICATION:

Replacement for the paragraph beginning at page 12, line 10:

Group 1: Eight animals receiving an infusion of NH_4Cl mixed with normal saline, at a constant rate of 12.3 $\mu mol \cdot kg^{-1} \cdot min^{-1}$ for 240 minutes, commencing after the baseline measurements (0 min). An infusion of α-KGA (Sigma Chemical Co, St Louis, MO, USA), dissolved normal saline, was started after the 60 min measurement, at a rate of 2.85 $\mu mol \cdot kg^{-1} \cdot min^{-1}$ during the first (60-120 min), 5.7 $\mu mol \cdot kg^{-1} \cdot min^{-1}$ during the second (120-180 min) and 11.4 $\mu mol \cdot kg^{-1} \cdot min^{-1}$ during the third (180-240 min) hour of infusion.

CLAIMS (with indication of amended or new):

Amended 1. A method of preserving bodily protein stores in a catabolic patient, comprising the concomitant administration of a pair of pharmaceutical agents consisting essentially of (a) at least one of α-ketoglutarate and α-ketoglutaric acid and (b) ammonium, the amounts of the pair being effective to preserve skeletal muscle.

Amended 2. The method of claim 1, wherein the administration of (a) or (b) or both lasts for more than one hour.

Amended 4. The method of claim 2, wherein the concomitant administration lasts for more than 6 hours but less than 36 hours.

Amended 7. The method of claim 6, wherein the amount of infusion administrated of (a) is from 0.02 $\mu mol \cdot kg^{-1} \cdot min^{-1}$ to 30 $\mu mol \cdot kg^{-1} \cdot min^{-1}$.

Amended 8. The method of claim 7, wherein the amount of infusion administrated of (a) is from 0.5 $\mu mol \cdot kg^{-1} \cdot min^{-1}$ to 15 $\mu mol \cdot kg^{-1} \cdot min^{-1}$.

Amended 9. The method of claim 6, wherein the amount of infusion administrated of NH_4^+ is from 0.5 $\mu mol \cdot kg^{-1} \cdot min^{-1}$ to 20 $\mu mol \cdot kg^{-1} \cdot min^{-1}$.

Amended 10. The method of claim 9, wherein the amount of infusion administrated of NH_4^+ is from 1 $\mu mol \cdot kg^{-1} \cdot min^{-1}$ to 10 $\mu mol \cdot kg^{-1} \cdot min^{-1}$.

Amended 11. The method of claim 9, wherein the amount of infusion administrated of NH_4^+ is increased over the period of administration.

Amended 12. The method of claim 11, wherein the amount of infusion administrated of (a) is from 0.02 $\mu mol \cdot kg^{-1} \cdot min^{-1}$ to 30 $\mu mol \cdot kg^{-1} \cdot min^{-1}$.

Amended 15. A pharmaceutical dosage unit comprising a first pharmaceutical composition comprising at least one of α-ketoglutarate and α-ketoglutaric acid in a pharmaceutically acceptable carrier and a second pharmaceutical composition comprising ammonium in a pharmaceutically acceptable carrier, in an amount effective to preserve skeletal muscle.

Amended 16. The unit of claim 15, wherein both carriers are an infusion carrier.

Amended 17. The unit of claim 15, wherein both carriers are an oral carrier.

Amended 18. The unit of claim 15, wherein the α-ketoglutarate is in form of its sodium salt.

Amended 19. The unit of claim 15, wherein ammonium is in form of its chloride.

New 20. A method of preserving bodily protein stores in a catabolic patient, comprising the concomitant administration (a) at least one of α-ketoglutarate and α-ketoglutaric acid and (b) ammonium chloride in an amount effective to preserve skeletal muscle.

New 21. The method of claim 20, wherein the administration of (a) or (b) or both lasts for more than one hour.

APPENDIX B

VERSION WITH MARKINGS TO SHOW CHANGES MADE
37 C.F.R. § 1.121(b)(iii) AND (c)(ii)

SPECIFICATION:

Paragraph at page 12, line 10 to page 12, line 16:

Group 1: Eight animals receiving an infusion of [NH4Cl] NH_4Cl mixed with normal saline, at a constant rate of 12.3 $\mu mol \cdot kg^{-1} \cdot min^{-1}$ for 240 minutes, commencing after the baseline measurements (0 min). An infusion of α-KGA (Sigma Chemical Co, St Louis, MO, USA), dissolved normal saline, was started after the 60 min measurement, at a rate of 2.85 $\mu mol \cdot kg^{-1} \cdot min^{-1}$ during the first (60-120 min), 5.7 $\mu mol \cdot kg^{-1} \cdot min^{-1}$ during the second (120-180 min) and 11.4 $\mu mol \cdot kg^{-1} \cdot min^{-1}$ during the third (180-240 min) hour of infusion.

CLAIMS:

1. A method of preserving bodily protein stores in a catabolic patient, comprising the concomitant administration of a pair of pharmaceutical agents consisting essentially of (a) at least one of α-ketoglutarate and α-ketoglutaric acid and (b) ammonium, the amounts of the pair being [in an amount] effective to preserve skeletal muscle.

2. The method of claim 1, wherein the administration of (a) or (b) or both lasts for more than one hour.

4. The method of claim [3] 2, wherein the concomitant administration lasts for more than 6 hours but less than 36 hours.

7. The method of claim 6, wherein the [dosing rate] amount of infusion administrated of (a) is from 0.02 $\mu mol \cdot kg^{-1} \cdot min^{-1}$ to 30 $\mu mol \cdot kg^{-1} \cdot min^{-1}$.

8. The method of claim 7, wherein the [dosing rate] amount of infusion administrated of (a) is from 0.5 $\mu mol \cdot kg^{-1} \cdot min^{-1}$ to 15 $\mu mol \cdot kg^{-1} \cdot min^{-1}$.

9. The method of claim 6, wherein the [dosing rate] amount of infusion administrated of NH_4^+ is from 0.5 $\mu mol \cdot kg^{-1} \cdot min^{-1}$ to 20 $\mu mol \cdot kg^{-1} \cdot min^{-1}$.

10. The method of claim 9, wherein the [dosing rate] amount of infusion administrated of NH_4^+ is from 1 $\mu mol \cdot kg^{-1} \cdot min^{-1}$ to 10 $\mu mol \cdot kg^{-1} \cdot min^{-1}$.

11. The method of claim 9, wherein the [dosing rate] amount of infusion administrated of NH_4^+ is increased over the period of administration.

12. The method of claim 11, wherein the [dosing rate] amount of infusion administrated of (a) is from 0.02 $\mu mol \cdot kg^{-1} \cdot min^{-1}$ to 30 $\mu mol \cdot kg^{-1} \cdot min^{-1}$.

15. A pharmaceutical dosage unit comprising [The combination of] a first pharmaceutical composition comprising at least one of α-ketoglutarate and α-ketoglutaric acid in a pharmaceutically acceptable carrier and a second pharmaceutical composition comprising ammonium in a pharmaceutically acceptable carrier, in an amount effective to preserve skeletal muscle.

16. The [combination] unit of claim 15, wherein [the carrier is] both carriers are an infusion carrier.

17. The [combination] unit of claim 15, wherein [the carrier is] both carriers are an oral carrier.

18. The [combination] unit of claim 15, wherein the α-ketoglutarate is in form of its sodium salt.

19. The [combination] unit of claim 15, wherein ammonium is in form of its chloride.